FDA hearings confirm risks of antidepressants

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Testimony presented by experts at the first day of hearings held by the US Food and Drug Administration confirmed that depressed children who are treated with antidepressants are more likely to harm themselves than depressed children treated with placebo.

The hearings are being held jointly by the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee. Preliminary risk data on the use of antidepressant drugs in paediatric patients were presented at a joint meeting of two FDA committees on 2 February. Since that meeting, experts in suicidal behaviour in children assembled by Columbia University have independently classified the risks and the FDA has conducted an analysis of these data.

The analysis found that an earlier report carried out by Dr Andrew Mosholder of the FDA's Office of Drug Safety was justified. The Mosholder report, which evaluated data from 22 studies using nine drugs, was not published by the FDA when it was produced earlier this year, on the grounds that the reliability of events deemed to be "suicide related" were uncertain (7 August, p 307).

Dr Tarek Hammad of the FDA's Center for Drug Evaluation and Research said that Dr Mosholder's earlier conclusion that antidepressants were associated with an increased risk of self harm was justified

"Out of 100 patients treated, we might expect two to three patients to have some increase in suicidality due to short term treatment beyond the risk that occurs with the [depression]," concluded Dr Hammad.

Dr Wayne Goodman, chairman of the Psychopharmacologic Drugs Advisory Committee, told the hearing the results are "the opposite of what we'd expect."

The FDA analysis by Dr Hammad included data from the treatment of adolescent depression study (TADS)—making a total of 24 studies analysed by the FDA.

Dr John March, lead author of the TADS study as published in *JAMA* (2004;292:807), presented data to the committee from TADS that he said showed that the benefits of fluoxetine (Prozac), particularly in combination with cognitive behaviour therapy, outweighed the risks. Fluoxetine is the only drug approved for the treatment of adolescent depression in the United States and the United Kingdom.

Dr Goodman challenged Dr March about the lack of efficacy seen in TADS on a key primary end point, the children's depression rating scale, and asked whether, on the basis of the TADS data, fluoxetine would be able to be approved by the FDA for use in depression. Dr March answered that "technically" fluoxetine would not meet FDA criteria for approval but added that other end points were positive, indicating benefit.

The hearings, convened to assist the FDA in making possible regulatory recommendations, included extensive and often emotional testimony by the public. Parents of children who had hung, shot, or stabbed themselves to death spoke with voices cracking about how their children had become agitated or unable to sleep after beginning antidepressant treatment—symptoms they often attributed to akathisia, a side effect of the antidepressants that they said drove their children to suicide.

Other parents read testimony from their children saying that they were doing well only because of the antidepressants they were taking (and in some instances only alive because of them).

Dr Goodman, saying that it seemed that many children have benefited from antidepressants, commented, "However, the data supporting that observation is rather elusive." □

Officials reject claims of drug industry's influence

Ray Moynihan *London*

Questioned repeatedly about the effect of the drug industry on doctors' prescribing, medical education, scientific research, and drug evaluation, government officials told a parliamentary inquiry last week that there was no evidence of unhealthy influence.

Four senior officials from the Department of Health and one from the Department of Trade and Industry were giving evidence at the first public hearing of the far reaching inquiry of the House of Commons Health Committee into the industry's influence on the health system.

Committee chairman David Hinchliffe, who is soon to retire, told the *BMJ* that a key reason for the inquiry was the failure of the system as a whole to take public health and prevention sufficiently seriously. "What we want to look at is the way in which the curative role of industry might impact on policy development," he said.

The packed hearing of the committee opened last Thursday in Westminster with a question to the departmental officials asking why their written submission did not seem to acknowledge the industry's extensive influence over the system and whether they held opinions on that influence.

The health department's Dr Felicity Harvey launched into a defence of the industry, citing its £12bn ($22bn; €18bn) in annual exports and its trade surplus of more than £3bn.

Rather than the industry having any unhealthy influence, argued Dr Harvey, the government was successfully influencing the industry to do the right thing by patients and public health: drug company representatives were giving doctors good information, and rising numbers of prescriptions for antidepressants and drugs for heart problems were a sign that the government's health priorities were being adhered to.

As for any alleged promotional excesses, the officials stressed that all was under control. "We do have mechanisms in place," said Dr Harvey, the most senior official with responsibility for the government's relationship with the drug industry.

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David Hinchliffe said MPs wanted to consider whether the influence of the drug industry meant that the NHS concentrated too much on cure rather than prevention

Jon Owen Jones (Labour MP for Cardiff Central) asked Dr Harvey directly whether she understood that there was a fundamental conflict between the industry's drive for profit and the government's responsibility for public health. She replied that the "stakeholder relationship" between government and industry "brings many gains and many innovative medicines… with huge impacts on health outcomes."

The approach of the government officials appeared to rankle committee members, who have received written submissions and evidence that indicate widespread drug industry influence over many aspects of the health system.

Dr Richard Taylor (independent MP for Wyre Forest), said that he thought the officials had shown "complacency." "The government officials gave the impression industry influence is not a problem," said Dr Taylor. "I'm not sure that's right."

Dr Taylor told the *BMJ*, "There is a feeling among many members of parliament that the drug industry has much greater influence over the national health system than it should have. It decides where the research goes—and that's where treatment goes." □